

What is claimed is:

- 5 1. A single-chain multiple antigen-binding molecule comprising:
(a) a variable domain of a heavy chain of an immunoglobulin (VH) with a first specificity (A), or functional parts thereof,
(b) a variable domain of a light chain of an immunoglobulin (VL) with a second specificity (B), or functional parts thereof,
(c) a variable domain of a heavy chain of an immunoglobulin (VH) with the specificity (B), or functional parts thereof, and
10 (d) a variable domain of a light chain of an immunoglobulin (VL) with the specificity (A), or functional parts thereof,
wherein the VH and VL domains are connected in the form of a VH-VL construct or VL-VH construct, and wherein the two VH-VL constructs are connected via a peptide (P).
- 15 2. A single-chain multiple antigen-binding molecule as claimed in claim 1, which comprises more than two VH-VL constructs.
3. A single-chain multiple antigen-binding molecule as claimed in claim 1, which consists of two VH-VL constructs.
- 20 4. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the VH-VL constructs are connected via domains with the same specificity.
5. A single-chain multiple antigen-binding molecule as claimed in claims 1, wherein the specificities (A) and (B) are essentially identical.
- 25 6. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the VH and VL domains are connected via a peptide linker (L) in the form of a VH-L-VL construct or VL-L-VH construct.
7. A single-chain multiple antigen-binding molecule as claimed in claim 6, wherein the linker (L) is about 1-20 amino acids long.
- 30 8. A single-chain multiple antigen-binding molecule as claimed in claim 7, wherein the linker (L) is about 1-5 amino acids long.

9. A single-chain multiple antigen-binding molecule as claimed in claim 8, wherein the linker (L) comprises the amino acid sequence GGGGS.

10. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the peptide (P) is about 12-40 amino acids long.

5 11. A single-chain multiple antigen-binding molecule as claimed in claim 10, wherein the peptide (P) is about 12-20 amino acids long.

12. A single-chain multiple antigen-binding molecule as claimed in claim 11, wherein the peptide (P) is 14 amino acids long.

10 13. A single-chain multiple antigen-binding molecule as claimed in claim 10, wherein the peptide (P) comprises the amino acid sequence GGGGSGGRASGGGS^(SEQ ID NO: 2) or GGGGSGGRASGGGS^(SEQ ID NO: 3).

14. A single-chain multiple antigen-binding molecule as claimed in claim 13, wherein the peptide (P) has an amino acid sequence selected from the group consisting of GGGGSGGRASGGGS^(SEQ ID NO: 2) and GGGGSGGRASGGGS^(SEQ ID NO: 3).

15. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein said molecule further comprises an effector (E).

16. A single-chain multiple antigen-binding molecule as claimed in claim 15, wherein the effector (E) is linked to said molecule via a connector (B).

20 17. A single-chain multiple antigen-binding molecule as claimed in claim 16, wherein the connector (B) comprises a protease cleavage sequence.

25 18. A single-chain multiple antigen-binding molecule as claimed in claim 17, wherein the protease cleavage sequence is selected from the group consisting of PSA, cathepsin, plasminogen and plasminogen activator cleavage sequence.

19. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the first specificity (A) is directed against a molecule to be analysed, and the second specificity (B) is directed against an analyte.

20. A single-chain multiple antigen-binding molecule as claimed in claim 19, wherein the analyte is selected from the group consisting of a radioactive molecule, a fluorescent molecule and an enzyme.

21. A single-chain multiple antigen-binding molecule as claimed in claim 15, wherein the first specificity (A) is directed against a molecule to be analysed, the second specificity (B) is directed against another molecule to be analysed, and the effector (E) is an analyte.

22. A single-chain multiple antigen-binding molecule as claimed in claim 21, wherein the analyte is selected from the group consisting of a radioactive molecule, a fluorescent molecule and/or an enzyme.

23. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the peptide (P) further comprises a fusogenic peptide.

24. A single-chain multiple antigen-binding molecule as claimed in claim 15, wherein the effector (E) comprises a fusogenic peptide.

25. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the first specificity (A) is directed against a target cell, and the second specificity (B) is directed against a vector.

26. A single-chain multiple antigen-binding molecule as claimed in claim 25, wherein the vector is selected from the group consisting of a nucleic acid, a cationic peptide or protein, a cationic lipid, a cationic polymer, a cationic porphyrin and a viral vector selected from the group consisting of an AdV, AAV, vaccinia, RSV, HSV, influenza and lentivirus vector.

27. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the first specificity (A) is directed against a cell membrane.

28. A single-chain multiple antigen-binding molecule as claimed in claim 27, the cell membrane is selected from the group consisting of cell membrane

of lymphocytes, macrophages, monocytes, granulocytes, hematopoietic cells, endothelial cells, smooth muscle cells, striped muscle cells, epithelial cells, liver cells, kidney cells, glia cells, cells of the supporting tissue, tumor cells and leukemia cells.

5 29. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the first specificity (A) is directed against a protein.

10 30. A single-chain multiple antigen-binding molecule as claimed in claim 29, wherein the protein is selected from the group consisting of a protein of the extracellular matrix, of the complement system, of the coagulation system, of the kinin system, of the blood plasma, and of the supporting tissue.

31. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the first specificity (A) is directed against a cytokine or a chemokine.

15 32. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the first specificity (A) is directed against an endogenous or exogenous toxin.

33. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the first specificity (A) is directed against a pharmaceutical.

20 34. A single-chain multiple antigen-binding molecule as claimed in claim 33, wherein the pharmaceutical is digitalis.

35. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the first specificity (A) is directed against a pathogen.

25 36. A single-chain multiple antigen-binding molecule as claimed in claim 35, wherein the pathogen is a bacterial pathogen, a viral pathogen, or a parasitic pathogen.

37. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the second specificity (B) is directed against a cell membrane.

38. A single-chain multiple antigen-binding molecule as claimed in claim 37, wherein the cell membrane is selected from the group consisting of a cell membrane of lymphocytes, macrophages, monocytes, and granulocytes.
39. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the second specificity (B) is directed against a protein.
40. A single-chain multiple antigen-binding molecule as claimed in claim 39, wherein the protein is selected from the group consisting of a protein of the complement system, of the coagulation system, and a fibrinolytic protein.
41. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the second specificity (B) is directed against a cytokine, a chemokine or a growth factor.
42. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the second specificity (B) is directed against an endogenous or exogenous toxin.
43. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the second specificity (B) is directed against a pharmaceutical.
44. A single-chain multiple antigen-binding molecule as claimed in claim 43, wherein the pharmaceutical is digitalis.
45. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the second specificity (B) is directed against a pathogen.
46. A single-chain multiple antigen-binding molecule as claimed in claim 45, wherein the pathogen is a bacterial pathogen, a viral pathogen, or a parasitic pathogen.
47. A single-chain multiple antigen-binding molecule as claimed in claim 1, wherein the second specificity (B) is directed against an enzyme that is able to convert the inactive precursor of a drug into an active, particular cytotoxic drug, on the target structure.

48. A single-chain multiple antigen-binding molecule as claimed in claim 1,
wherein the second specificity (B) is directed against a peptide hormone
or a steroid hormone.
49. A single-chain multiple antigen-binding molecule as claimed in claim 1,
wherein the second specificity (B) is directed against a constant part of an
immunoglobulin.
50. A single-chain multiple antigen-binding molecule as claimed in claim 1,
wherein the second specificity (B) is directed against a mediator.
51. A single-chain multiple antigen-binding molecule as claimed in claim 50,
wherein the mediator is selected from the group consisting of the
mediator histamine, serotonin, leukotrine, prostacyclin and kinin.
52. A single-chain multiple antigen-binding molecule as claimed in claim 1,
wherein the second specificity (B) is directed against a tumor cell.
53. A single-chain multiple antigen-binding molecule as claimed in claim 15,
wherein the effector (E) is selected from the group consisting of a
transmembrane domain, a glycopospholipid anchor, the ligand-binding
part of a receptor, a ligand for a receptor, the receptor-binding part of a
ligand, a peptide hormone, a cytokine, a growth factor, a growth factor
inhibitor, a chemokine, an interferon, a mediator, a peptide acting on the
circulation, an enzyme which converts an inactive precursor of a drug into
an active drug, a protein which activates coagulation, a protein which
inhibits coagulation, a protein which activates fibrinolysis, a protein which
inhibits fibrinolysis, a protein which activates the complement system, a
protein which inhibits the complement system, a constant domain of an
immunoglobulin, a cytotoxic peptide, a single-chain antigen-binding
molecule, a tumor antigen, an antigen of a pathogen, a peptide
comprising cysteine, and a di- or multimerizing peptide.
54. A single-chain multiple antigen-binding molecule as claimed in claim 53,
wherein the effector is an antigen of a pathogen and is selected from the group
consisting of a bacterial antigen and a viral antigen.

55. A single-chain multiple antigen-binding molecule as claimed in claim 53,
wherein the effector is a single-chain antigen binding molecule and is
selected from the group consisting of a single-chain antigen binding
molecule with single antigen binding capacity, a single-chain antigen
binding molecule with double antigen binding capacity and single-chain
antigen binding molecule with multiple antigen binding capacity.
56. A recombinant nucleic acid molecule coding for a single-chain multiple
antigen-binding molecule as claimed in 1.
57. The nucleic acid as claimed in claim 56, further comprising at the 5' end a
nucleotide sequence coding for a transmembrane sequence.
58. The nucleic acid as claimed in claim 56, further comprising at the 5' end a
nucleotide sequence coding for a signal sequence.
59. A nucleic acid as claimed in claim 56, wherein said nucleic acid further
comprises at the 5' end an operably linked promoter.
60. A nucleic acid as claimed in claim 56, wherein said nucleic acid further
comprises at the 5' end a transcription activator binding sequence.
61. A nucleic acid as claimed in claim 60, wherein the activator is regulated
cell-specifically, cell cycle-specifically, metabolism-specifically or by a
drug.
62. A nucleic acid as claimed in claim 59, wherein said nucleic acid further
comprises at the 5' end of the start codon the sequence GCCACC₂ or
GCCGCC₂ (SF2 FD NO: 18)
63. A vector comprising a nucleic acid as claimed in claim 56.
64. A vector as claimed in claim 63, wherein the vector is a viral vector.
65. A vector as claimed in claim 63, wherein the vector is a nonviral vector.

66. A vector as claimed in claim 65, wherein the nonviral vector is selected from the group consisting of a cationic lipid, a cationic polymer, a cationic peptide and a cationic porphyrin.

67. A cell comprising a nucleic acid as claimed in claim 56.

5 68. A cell comprising a vector as claimed in claim 63.

69. A cell as claimed in claim 67, wherein the cell is a bacterial, yeast, insect or mammalian cell.

10 70. A cell as claimed in claim 69, wherein the mammalian cell is selected from the group consisting of a lymphocyte, a macrophage, a glia cell, an epithelial cell, a liver cell, a kidney cell, a bone marrow cell, an endothelial cell, a smooth muscle cell, a striped muscle cell, and a fibroblast.

71. A process for preparing a single-chain multiple antigen-binding molecule, which comprises cultivating a cell as claimed in claim 67 and isolating the expression product where appropriate.

15 72. A pharmaceutical composition comprising a single-chain multiple antigen-binding molecule as claimed in claim 1.

73. A pharmaceutical composition comprising a nucleic acid as claimed in claim 56.

74. A pharmaceutical composition comprising a vector as claimed in claim 63.

20 75. A pharmaceutical composition comprising a cell as claimed in 67.

76. A diagnostic aid comprising a single-chain multiple antigen-binding molecule as claimed in claim 19.

77. A diagnostic aid comprising a single-chain multiple antigen-binding molecule as claimed in claim 21.

Sub B'
25 78. A method for the diagnosis, prophylaxis or treatment of cancer, autoimmune diseases, inflammatory diseases, disorders of the blood,

disorders of the nervous system or infectious diseases using a single chain multiple binding molecule as claimed in claim 1.

- 5 79. A method for the diagnosis, prophylaxis or treatment of cancer, autoimmune diseases, inflammatory diseases, disorders of the blood, disorders of the nervous system or infectious diseases using a recombinant nucleic acid molecule as claimed in claim 56.
- 10 80. A method for the diagnosis, prophylaxis or treatment of cancer, autoimmune diseases, inflammatory diseases, disorders of the blood, disorders of the nervous system or infectious diseases using a vector as claimed in claim 63.
81. A method for the diagnosis, prophylaxis or treatment of cancer, autoimmune diseases, inflammatory diseases, disorders of the blood, disorders of the nervous system or infectious diseases using a cell as claimed in claim 67.
- 15 82. A method according to claim 72, wherein the cell is injected into a patient intravenously, intra-arterially, into a body cavity, into an organ or subcutaneously.

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